DEVICE FOR DIVIDING CELL MASS, AND METHOD FOR DIVIDING CELL MASS USING SAME

TECHNICAL FIELD

[0001] The present invention relates to a device for dividing cell aggregates, and a method for dividing cell aggregates by using the device.

BACKGROUND ART

[0002] In recent years, a cell culture method (also called a suspension culture method) has been developed in which various cells such as pluripotent stem cells and the like are suspended in a liquid medium and three-dimensionally grown into a cell aggregate (e.g., patent document 1 and the like). In addition, a liquid medium for preferably performing the suspension culture method and a production method thereof have also been developed (e.g., patent document 2 and the like).

[0003] In suspension culture method, the undifferentiated state of pluripotent stem cells may decrease as the cell aggregate grows larger. For example, non-patent document 1 suggests that the undifferentiated state of large cell aggregates of 150 μm or more may decrease.

[0004] On the other hand, in the culture method of pluripotent stem cells described in patent document 1, pluripotent stem cells are suspension cultured until they become large cell aggregates having an average diameter of about 200-about 300 μm, the obtained large cell aggregates are divided into smaller cell aggregates having an average diameter of about 80 to about 120 μm, after which suspension culture is further continued to maintain and amplify the pluripotent stem cells. In this culture method, a mesh made by knitting nylon or metal wire is used as a specific method for dividing large cell aggregates, and large cell aggregates are passed through the mesh to be divided into small cell aggregates corresponding to the mesh-holes (square pass holes) of the mesh.

DOCUMENT LIST

Patent Documents

[0005] patent document 1: WO 2013/077423

[0006] patent document 2: WO 2016/163444

Non-Patent Document

[0007] non-patent document 1: Andreas Elanzew et al., "A reproducible and versatile system for the dynamic expansion of human pluripotent stem cells in suspension", Biotechnology Journal, 2015, 10, 1589-1599.

SUMMARY OF INVENTION

Technical Problem

[0008] However, when the present inventors have examined in detail the division of the cell aggregates using the mesh as described above, it was found that the cell aggregates passing through the mesh may not be preferably divided due to the structure peculiar to the mesh. The mesh is a kind of sheet-like material, and when the sheet surface is seen macroscopically in a straight view, the warp wire and the weft wire appear to intersect linearly as shown in FIG. **10**(*a*), and the mesh-hole also looks like a flat plane square. However, when each mesh-hole is microscopically observed, since the warp wire and the weft wire are knitted three-dimensionally so as to avoid each other, four wires (two warp wires (**101**, **102**) and two weft wires (**111**, **112**)) constituting four sides surrounding one square mesh-hole **100** wave broadly in the thickness direction of the mesh as shown in FIG. **10**(*b*).

[0009] When cell aggregates pass through such mesh-hole surrounded by four wavy wires, since the cross-sectional shape of each wire is a circular shape, and the surface of the wire body is a curved surface, the cell aggregates may not be divided appropriately or sharply in some cases. When a thinner wire is used to improve such defect of the mesh, the strength of the mesh is reduced. When this is improved by increasing the wire strength, the mesh becomes more expensive. When cell aggregates are divided by a mesh formed using a wire and the flow velocity of a liquid medium is low, the cell aggregates cannot be cut but are only trapped in the mesh of the net. As a result, dividing and culture cannot be repeated and the collection rate of the cell aggregates becomes low. Therefore, a certain level of high flow velocity is necessary. On the other hand, when the flow velocity of a liquid medium is high, the divided cell aggregates receive a shear due to the high-speed flow and become smaller. It is not preferable to divide cell aggregates of pluripotent stem cells to have an outer diameter of 40 μm or less, since the cells are significantly damaged as evidenced by apoptosis of the cell and the like.

[0010] As described above, when cell aggregates are divided using a conventional mesh, a low flow velocity of a liquid medium leads to a low cell recovery rate and a high flow velocity of a liquid medium leads to large damage on the cell aggregates and low expansion culture efficiency.

[0011] The present invention aims to provide a device that can solve the above-mentioned problem and divide cell aggregates more preferably, and a method for dividing cell aggregates by using the device.

Solution to Problem

[0012] The present inventors have conducted intensive studies in an attempt to solve the above-mentioned problems and found that a porous film having many through-holes disposed on the film surface to form mesh-holes, and a beam part having a sharp corner, compared with mesh wires, on the body surface is free from waving of the beam part surrounding the through-holes and can cut cell aggregates more preferably, which resulted in the completion of the present invention.

[0013] The main constitution of the present invention is as follows.

[0014] [1] A device for dividing a cell aggregate into smaller cell aggregates, the device comprising a film-like main body part, wherein

[0015] a predetermined region on a film surface of the main body part has a mesh structure with many through-holes disposed on the film surface, the mesh structure comprises many through-holes penetrating the predetermined region in the film thickness direction, and a beam part serving as a partition between the through-holes,

[0016] the through-holes have an opening shape of a size permitting passage of the aforementioned smaller cell aggregates,